INDIAN HEART JOURNAL 66 (2014) 249–250

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Letters to the Editor

Letter to the Editor for sponsored article "Pharmacologic reperfusion therapy with indigenous tenecteplase in 15,222 patients with ST elevation myocardial infarction – the Indian registry" by Iyengar et al

I read with great interest the article by Iyengar et al[1] examining the efficacy and safety of indigenous tenecteplase such as used in the real world in India. The figures reported are impressive, with 15,222 consecutive patients included in 722 centers, as well as striking clinical results. I have, however, several comments and interrogations regarding the study.

First, there is no mention of whether the patients were asked to give informed consent for their participation in the registry, and whether the study was approved by an ethics committee.

Second, the population is described as a consecutive population of patients receiving indigenous tenecteplase; how many patients admitted to the participating institutions during the study period of recruitment did not get tenecteplase, and what was their clinical profile in comparison with that of the registry patients?

Third, the main efficacy criterion, clinically successful thrombolysis, is of an extremely subjective nature: what is "significant relief of chest pain" and "significant resolution of ST-segment elevation"? Was chest pain quantified in any way, and was there any central reading of the ECGs? At what time with respect to the time of administration of indigenous tenecteplase was clinical success assessed? (In the end chest pain resolves in all AMI patients!). This question is central to the interpretation of the results presented here, as this is a purely observational study, where the subjective interpretation of success by the participating clinicians is most likely to explain the properly extraordinary success rate reported in the article. It is somewhat surprising that the authors failed to report initial TIMI flow of the culprit artery in the small proportion of patients who underwent coronary angiography.

Fourth, the way the complication rates are presented for subgroups is not proper: comparisons should not be made with the rates observed in the overall population, as it contains the subgroup of interest. The ways the results presented here preclude any statistical analysis.

Finally, the overall clinical complication rates observed are most likely explained by the very young age of the population (55 years on average, with 8% only aged >70 years). In such young STEMI patients, 30-day mortality is extremely low, even in the absence of any reperfusion therapy. In the FAST-MI 2010 registry,[2] the mortality of patients less than 70 years of age (and with an average age of 55 years) was 1.80% for those who received no reperfusion therapy, compared with 0.4% for those treated with fibrinolytic therapy (mainly original tenecteplase) and 1.0% for those receiving primary PCI (personal data).

Because of all these limitations, strong conclusions such as "this study establishes the efficacy of a thrombolytic like TNK in prompt and effective reperfusion of the myocardium" are inappropriate. Only specifically designed, randomized controlled clinical trials can truly establish the efficacy of any therapy. Observational data can only show associations and it is essential that clinicians refrain from drawing hasty causality inferences from such data.[3]

Disclosures

N. Danchin has received research grants from: AstraZeneca, Daiichi-Sankyo, Eli-Lilly, GSK, MSD, Novartis, Pfizer, Servier, Sanofi. Fees for lectures: AstraZeneca, Boehringer-Ingelheim, Daiichi-Sankyo, Eli-Lilly, Novo-Nordisk, Sanofi, Servier, The Medicines Company. Consulting fees: AstraZeneca, Bayer, Daiichi-Sankyo, Eli-Lilly, Novo-Nordisk, Sanofi, Servier.

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0019-4832/$ – see front matter

http://dx.doi.org/10.1016/j.ihj.2014.02.001

Rejoinder

We thank the corresponding author/authors for the interest in the article[1] and the comments.

[1] This publication is a compilation of observations made by physicians in treating their patients of ST Elevation Myocardial Infarction (STEMI) with the indigenous tenecteplase. It is a registry which is observational, non-interventional and retrospective in nature. Patient identity was not revealed. Hence there was no requirement for informed consent or ethics committee approval.

[2] Records of patients who received the indigenous tenecteplase only were compiled. Records of other patients were not compiled or evaluated.

[3] Clinically successful thrombolysis was judged by (a). Resolution of chest pain & (b) 50% ST segment resolution at 90 minutes. Pain relief assessment was subjective and was noted as Yes/No. No pain scale was used. There was no central ECG monitoring.

The study did not look at the angiographic profile. However a sub study is being planned to look into the angiographic patency rates and TIMI flow.

[4] Analysis was done comparing the overall group with the high risk subgroups, as also between subgroups (elderly vs nonelderly; diabetics vs nondiabetics; male vs female) ref. Fig 4 in the article.[1]

[5] We fully agree with the author's contention that the young age of the population might have been responsible for the low mortality figures. However, divergent data (including time of presentation, delay of thrombolysis) complicate the issue. In the Fibrinolytic Therapy Trialists (FTT) collaborative group data,[2] the overall 30-day mortality in the age group less than 55 years was 4.6% in the control group and 3.4% in the thrombolysed group.

The figures quoted by the corresponding author show substantial relative risk reduction in young STEMI patients who received reperfusion therapy. Indian patients are known to get Acute Coronary Syndrome (ACS) at a younger age than their western counterparts.

Randomized Clinical Trials (RCT) is certainly the gold standard in clinical trials. But observational registry data reflect real life scenario. The debate of superiority of each is an open and ongoing academic debate. We need to use the "registries to investigate the past and develop the future".[3] Well designed post-marketing surveillance registries can be used to prove safety and efficacy in a broad spectrum of patients.[4]

The whole purpose of this registry was to examine the efficacy and safety of a low cost indigenous tenecteplase in a financially challenged heterogenous population of India.

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Available online 4 March 2014

DOI of original article: http://dx.doi.org/10.1016/j.ihj.2014.02.001.

0019-4832/$ – see front matter

http://dx.doi.org/10.1016/j.ihj.2014.02.013